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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/964,114	09/25/2001	Hans P. Albrecht	BBI-5035CPUSDV	2006

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EXAMINER	
BORIN, MICHAEL L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 03/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/964,114	ALBRECHT ET AL.	
	Examiner	Art Unit	
	Michael Borin	1631	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *1,11,20,22,24,25,27,29,32-41,49,51 and 53-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-10,12-19,21,23,26,28,30,31,42-48,50,52 and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-58 are pending.

Response to restriction requirement filed 11/24/2003 is acknowledged. Applicant elected, with traverse, Group II. Applicant argues that methods of groups IV-IX should be rejoined with group II, because they are all subgeneric to group II as they all include common mechanism. Examiner disagrees. Unlike amended claims 2-10,12-18,28,30,31,42-47,50,52,58 which are amended to depend on claims drawn to inhibition of ICE, methods of Groups IV-XI do not address ICE inhibition and as such are drawn to independent methods of treatment of disorders that have different mechanisms of development and etiology, in addition to the methods of treatment having different enablement requirements. The restriction requirement is still deemed proper and is therefore made FINAL. Claims 2-10,12-18,21,23,28,30,31,42-47,50,52,58 are rejoined with the claims 19,26,48 of Group II, and claims 1,11,20,22,24,25,27,29,32-41,49,51,53-57 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected groups. Cancellation of claims 1,11,20,22,24,25,27,29,32-41,49,51,53-57 is requested.

Title, Abstract

The title and abstract of the invention are not descriptive. The title and abstract do not reflect the elected invention. A new title and abstract are required which are clearly indicative of the invention to which the elected claims are directed.

Specification

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Claim Objections

Claim 2: place period at the end of the claim.

Claim 17: after "wherein" delete "is".

Claim Rejections - 35 USC § 112, first paragraph.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-10,12-19,21,23,26,28,30,31,42-48,50,52,58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *in vitro* inhibition of ICE, does not reasonably provide enablement for *in vivo* inhibition of the enzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to method of inhibiting ICE *in vivo*.

Prior art teaches that in regard to *in vivo* effect of ICE inhibitors, "a number of formidable questions remain regarding [ICE] regulation and mechanism of activation. Answering these questions experimentally will present a major challenge due to the extremely low levels of enzyme present in cells." See Tocci et al. (Database Medline, AN 97340742. Vitamins and hormones, (1997) 53, 27-63). Further, the reference teaches that it still remains to be determined what level of inhibitor is required for a therapeutic effect, and that, because of growing number of members of ICE family, a putative *in vivo* inhibitor should demonstrate selectivity for ICE while retaining potency. None of these issues is addressed in the instant specification asserting the *in vivo effect.*

Specification does demonstrate effect of exemplary compounds on ICE and caspase-4 in *in vitro* experiments but does not provide any data on *in vivo* effect of the

inhibitors. Specification offers general guidance on administration of the inhibitors (pages 13-15); however, this guidance offers a dosage range of four orders of magnitude (p. 15, lines 11-15), and does not specify for which of multiple ways of administration this range is suitable. Although the specification provides a dosage range for administration of ICE inhibitors, there is no standard by which to measure whether the compound will operate as intended. There are no guidelines for determination of dosage needed to provide treatment of one ICE-related disorder *vs* another (e.g., septic shock *vs* Alzheimer's disease). Furthermore, the range of 0.01-100 mg/kg/day suggested by the specification, amounts to the concentration range of 0.014-14 mkm (considering an average body weight of 70 kg, and average molecular weight of an inhibitor as 500g). This required concentration will not be achieved by majority of inhibitors illustrated in Table 1, as their *in vitro* inhibitory concentration is higher - see data for compounds 2b-2k, for example.

In view of the above, it is the Examiners position that with the insufficient guidance and working examples and in view of unpredictability and the state of art one skilled in the art could not make and/or use the invention with the claimed breadth without an undue amount of experimentation.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0549.

March 2, 2004

MICHAEL BORIN, PH.D
PRIMARY EXAMINER

mlb